LUX-Lung 7: is there enough data for a final conclusion?

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LUX-Lung 7: is there enough data for a final conclusion?

We read with great interest the publication of the LUX-Lung 7 trial,[1] comparing afatinib and gefitinib as first-line treatment of patients with advanced non-small-cell lung cancer with common EGFR mutations. As a general rule, in settings where more than one drug is available for the same treatment indication, a direct comparison is always useful. However, we believe that in the case of LUX-Lung 7, a complete evaluation of the comparison would need more details than those available in the publication in *The Lancet Oncology*.

First of all, final results of overall survival should have been presented within the primary publication. Albeit progression-free survival has been widely accepted as an endpoint in the first-line setting of patients positive for *EGFR* mutations **[A: correct edi of EGFR mutation positive cases?]**, overall survival was chosen by the authors as a coprimary endpoint together with progression-free survival and time-to-tre nt failure. Therefore **[A: edit ok?]** definitive interpretation of the results should be based on all coprimary endpoints.

Furthermore, the interpretation of the time-to-treatment failure advantage described in favour of afatinib is quite difficult, not only because of the open-label design of the trial, but also because of the absence of details about characteristics of disease progression in the two groups. In this setting, tyrosine-kinase inhibitors are commonly administered beyond the formal definition **[A: do you mean determination or assessment?]** of progression, especially in asymptomatic patients with oligo-progressive disease.[2] The longer time-to-treatment failure reported in patients treated with afatinib versus gefitinib compared with the negligible difference between groups in median progression-free survival documents a higher amount of treatment beyond progression with afatinib than with gefitinib. It would be of interest to see if this disparity in the administration beyond progression could be justified by different characteristics of disease at the time of progression according to the Response Evaluation Criteria in Solid Tumors. For instance, a significant difference in the proportion of symptomatic patients, as well as a significant difference in the number of progressing metastatic sites, or in the volumetric burden of progression, would represent a reasonable explanation for the time-to-treatment failure difference. Unfortunately, this information was not available in the publication. Additionally, the difference in median progression-free survival in favour of afatinib was very small (0·1 months) and clinically negligible.

In conclusion, based on the LUX-Lung 7 data published to date, it seems to us premature to claim that afatinib has definitely proven to be superior to gefitinib in this setting.

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1 Park K, Tan EH, O'Byrne K, et al. Afatinib versus gefitinib as first-line treatment of patients with EGFR mutation-positive non-small-cell lung cancer (LUX-Lung 7): a phase 2B, open-label, randomised controlled trial. *Lancet Oncol* 2016; published online April 12. http://dx.doi.org/10.1016/S1470-2045(16)30033-X.

2 Park K, Yu CJ, Kim SW, et al. First-line erlotinib therapy until and beyond response evaluation criteria in solid tumors progression in asian patients with epidermal growth factor receptor mutation-positive non-small-cell lung cancer: the ASPIRATION Study. *JAMA Oncol* 2016; **2:** 305–12.